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| EXAMINER | |
|---|---|
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| ART UNIT | PAPER NUMBER |
| 1645 | |

DATE MAILED: 06/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/001,737 | MIZZEN ET AL. | |
| | Examiner | Art Unit | |
| | S. Devi, Ph.D. | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *15 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2,3,5-7,19-24,31,35 and 38* is/are pending in the application.

4a) Of the above claim(s) *4,8,32 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,5-7,19-24,31 and 38-45* is/are rejected.

7)☒ Claim(s) *33 and 35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

## RESPONSE TO APPLICANTS' AMENDMENT

### Applicants' Amendments

**1)** Acknowledgment is made of Applicants' amendments filed 12/11/03 and 03/15/04 in response to the non-final Office Action mailed 06/06/03. It is noted that the amendment filed 03/15/04 is non-compliant in the sense that claim 8 is indeed amended via this amendment, yet incorrectly identifies claim 8 as '(Previously amended)'.

### Status of Claims

**2)** Claims 4, 5, 19-24 and 31 have been amended via the amendment filed 12/11/03.

Claims 1, 9-18, 25-30, 36 and 37 have been canceled via the amendment filed 12/11/03.

New claims 40-45 have been added via the amendment filed 12/11/03.

Claims 2-8, 19-24, 31-35 and 38-45 are pending.

Claims 3(a), a part of 3(c), claim 4, a part of claims 5 and 6, claim 8, claims 32 and 34, a part of claims 38 and 39, claim 40(a), and a part of 40(c), and claims dependent therefrom or corresponding parts of such dependent claims are withdrawn from consideration as being directed to the 'further restricted' and the non-elected nucleic acid molecule of SEQ ID NO: 5. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

Claims 2, 3, 5-8, 19-24, 31, 33, 35 and 38-45, to the extent they encompass the elected nucleic acid molecule of SEQ ID NO: 7, are under examination.

### Prior Citation of Title 35 Sections

**3)** The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

### Prior Citation of References

**4)** The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

### Objection(s) Moot

**5)** The objection to claim 37 made in paragraph 17(a) of the Office Action mailed 06/06/03 is moot in light of Applicants' cancellation of the claim.

**6)** The objection to claims 4 and 8 made in paragraph 17(a) of the Office Action mailed

06/06/03 is moot in light of the fact that these claims are now drawn to non-elected invention.

**Objection(s) Withdrawn**

**7)** The objection to the drawings made in paragraph 6 of the Office Action mailed 06/06/03 is withdrawn in light of Applicants' submission of formal drawings submitted 02/11/04.

**8)** The objection to the specification made in paragraph 7 of the Office Action mailed 06/06/03 is withdrawn in light of Applicants' amendments to the specification.

**9)** The objection to claim 20 made in paragraph 17(b) of the Office Action mailed 06/06/03 is withdrawn in light of Applicants' amendment to the claim.

**Objection(s) Maintained**

**10)** The objection to claims 3, 5-7, 20, 33, 35, 38 and 39 made in paragraph 17(a) of the Office Action mailed 06/06/03 is maintained for reasons set forth thereon.

**Rejection(s) Moot**

**11)** The rejection of claims 4, 19-24 and 31 made in paragraph 14 of the Office Action mailed 06/06/03 under 35 U.S.C § 102(e) as being anticipated by Covacci *et al.* (US 6,077,706), is moot in light of Applicants' amendments to the base claim 4 to exclude the elected subject matter.

**12)** The rejection of claim 37 made in paragraph 16 of the Office Action mailed 06/06/03 under 35 U.S.C § 102(b) as being anticipated by Labigne *et al.* (WO 94/26901) is moot in light of Applicants' cancellation of the claim.

**13)** The rejection of claims 8 and 19-24 made in paragraph 16 of the Office Action mailed 06/06/03 under 35 U.S.C § 102(b) as being anticipated by Labigne *et al.* (WO 94/26901) is moot in light of Applicants' amendments to the base claim 8 to exclude the elected subject matter.

**Rejection(s) Withdrawn**

**14)** The rejection of claim 2 made in paragraphs 11(a) and 11(k) of the Office Action mailed 06/06/03 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn. Applicants refuse to amend the claim as suggested that would 'particularly point out and distinctly claim the subject matter which Applicants regard as the invention'. Instead, Applicants go on the record with the following statements.

Applicants contend that 'Hsp60' is not an abbreviation, but refers to proteins which, based on their structure and function, are within a particular hsp family, the Hsp60 family. Applicants submit a

review article which uses the term 'Hsp60'. Applicants state that Hsp60 is a term complete unto itself.

**15)** The rejection of claims 4 and 5 made in paragraph 11(b) of the Office Action mailed 06/06/03 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims.

**16)** The rejection of claim 3 made in paragraphs 11(c), 11(d), 11(e), 11(f), 11(g) and 11(k) of the Office Action mailed 06/06/03 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn. Applicants refuse to amend the claim as suggested that would 'particularly point out and distinctly claim the subject matter which Applicants regard as the invention'. Instead, Applicants go on the record with the following statements.

Applicants contend that the questioned phrase, for example in claim 6, "polypeptide comprising a sequence" (as opposed to --polypeptide comprising an amino acid sequence--) is preceded by the language 'isolated nucleic acid molecule comprising a nucleic acid sequence that encodes a polypeptide comprising a sequence'. Applicants assert that it is well understood that nucleic acid sequences encode amino acid sequences. Applicants state that amending one's claims even to a seemingly trivial extent can impact the way in which they are later interpreted. Applicants state that they are not inclined to make any amendment that simply makes more explicit what is already clear and readily understandable.

**17)** The rejection of claims 19 and 31 made in paragraph 11(h) of the Office Action mailed 06/06/03 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims.

**18)** The rejection of claim 23 made in paragraph 11(I) of the Office Action mailed 06/06/03 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

**19)** The rejection of claim 24 made in paragraph 11(j) of the Office Action mailed 06/06/03 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

**Rejection(s) Maintained**

**20)** The rejection of claims 5, 6, 19-24, 31, 38 and 39 made in paragraph 12 of the Office Action

mailed 06/06/03 under 35 U.S.C § 112, first paragraph, as containing inadequate written description, is maintained for reasons set forth therein and herebelow.

Applicants contend that the legal standard is, could one of ordinary skill in the art reasonably conclude that the inventors had possession of the claimed invention. Applicants cite parts of the *Written Description Guidelines* from the January 2001 *Federal Register* and state that possession may be shown in a variety of ways, which include description of an actual reduction to practice; and a showing that the invention was 'ready for patenting' such as by the disclosure of drawings or structural chemical formulas which show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. Applicants reproduce a part of the *Guidelines* from page 1105 that is related to 'the introduction of new matter'. Applicants further cite that part of the *Guidelines* which states that the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention claimed. With respect to the disclosure of species within a claimed genus, Applicants reproduce a part of the *Guidelines* from page 1106, which states that a 'representative number of species' means that the species which are adequately described are representative of the entire genus, and that when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. Applicants particularly note the statement in the *Guidelines* that satisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. Applicants acknowledge that the specification does indeed disclose diagnostic and vaccine intentions. Applicants however submit that it does not mean that they must demonstrate success with every single nucleic acid molecule claimed in every single indication disclosed, nor is the written description requirement satisfied only if Applicants write out all of the variants they claim. Applicants assert that they have adequately described those variants within the present specification in such a way that one of ordinary skill in the art would recognize that Applicants possessed not just some, but all of the variants claimed. With regard to the nucleic acid molecule claimed in claim 5, which nucleic acid molecule is required to comprise a sequence that is identical to a segment comprising at least 25% of

contiguous nucleotide bases of SEQ ID NO: 7 from nucleotides 15-1652', Applicants state that they provide the sequence of SEQ ID NO: 7 and one could use the simplest math to arrive at the claimed molecule. Applicants then point to pages 5 and 6 of the specification that provide support for the same or similar words recited in claim 5.

Applicants' arguments have been carefully considered, but are not persuasive. The claims reciting the 'comprising' and 'encoding' language read on complete gene sequences having the nucleotide of SEQ ID NO: 7 from nucleotides 15-1652 which nucleotide is from any source. Whether or not Applicants have provided the sequence species of SEQ ID NO: 7 is not the issue. As set forth previously, one of ordinary skill in the art could reasonably conclude that the inventors had possession of the nucleotide sequence species, SEQ ID NO: 7. The only functional nucleic acid species within the claimed genus that is adequately described is SEQ ID NO: 7 which encodes a functional amino acid sequence of SEQ ID NO: 8. This does not constitute adequate written description for the whole genus that includes nucleic acid variant species, such as, those comprising at least 25% of contiguous nucleotide bases of SEQ ID NO: 7 from nucleotides 15-1652, and those variants that encode a polypeptide that has an amino acid sequence which is at least 95% (claim 6), 97% (claim 38) and 98% (claim 39) homologous to SEQ ID NO: 8. With the exception of SEQ ID NO: 7 from nucleotides 15-1652, one of skill in the art cannot envision the detailed chemical structure of the encompassed nucleic acid molecules irrespective of the simplicity of the method of isolation (or simplicity of the math involved in counting off the nucleotides), absent precise description. As Applicants readily acknowledge, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The precise structure of a representative number of nucleic acid variants and segments are not sufficiently described in the instant application. Contrary to Applicants allegation, Applicants have not been required to demonstrate success with every single nucleic acid molecule claimed, but a representative number. The term 'at least' in the claims with regard to the percent homology allows innumerable nucleic acid variant species. The claimed genus encompasses partial nucleotide sequences, undisclosed nucleic acid molecules, and nucleic acid molecules yet to be discovered, and the disclosed structural features of the nucleic acid molecule of SEQ ID NO: 7 encoding the polypeptide consisting of SEQ ID NO: 8 does not constitute a substantial portion of the claimed genus. Absent

adequate written description disclosing a representative number of the nucleotide sequence variants from the claimed broad genus of nucleic acid molecules, the specification as originally filed fails to show that Applicants were 'in possession of the claimed invention' at the time of the filing of the instant application.

Applicants submit that regardless of the polypeptide they encode, the claimed fragment and variant sequences that differ from SEQ ID NO: 7 are useful as probes and primers. Claim 5 and dependent claims, however, recite a nucleic acid comprising a nucleotide sequence identical to a segment 'comprising' at least 25% contiguous nucleotide bases of SEQ ID NO: 7 from nucleotides 15-1652 or a complement thereof, which is not required to hybridize under any specific hybridization conditions to a nucleic acid molecule. There does not appear to be an adequate written description, in the originally filed specification, of the essential structural features of the claimed nucleic acid molecules, nor is there a correlation between a particular structure and function. As claimed currently, no function is required of this nucleic acid molecule. Even if it was required to hybridize to a nucleic acid molecule of SEQ ID NO: 7 from nucleotides 15-1652, the genus of nucleic acid molecules which would hybridize to a nucleic acid comprising a nucleotide sequence identical to a segment comprising at least 25% contiguous nucleotide bases of SEQ ID NO: 7 from nucleotides 15-1652 or a complement thereof, is quite large, encompassing not only nucleotide sequences having polymorphisms and mutations compared to SEQ ID NO: 7 from nucleotides 15-1652, but also sequences having no common sequence with SEQ ID NO: 7 from nucleotides 15-1652 itself since hybridization can occur within the non-SEQ ID NO: 7 portion of the nucleic acid molecule that 'comprises' SEQ ID NO: 7 from nucleotides 15-1652 or encoding the polypeptide of SEQ ID NO: 8. Thus, the genus of nucleic acid molecules encompassed by the claim is quite extensive and there does not appear to be a requirement for a specific structure, a specific function, nor a correlation between a specific structure and a specific function. Again, the nucleic acid molecule of SEQ ID NO: 7 from nucleotides 15-1652 does not constitute a substantial portion of the claimed genus.

With regard to Applicants' assertion that the claimed fragment and variant sequences are useful as primers, neither member of the primer pair is limited to a fragmentary sequence contained within SEQ ID NO: 7 from nucleotides 15-1652. Instead, the open claim language of the claims means that primer pairs outside the sequence of SEQ ID NO: 7 from nucleotides 15-1652 are

encompassed by the instant claims. Thus, the genus of nucleic acid molecules useful as primers is large and the fragments present within SEQ ID NO: 7 from nucleotides 15-1652 that could serve as primer pairs to amplify a fragment of SEQ ID NO: 7 from nucleotides 15-1652 do not appear to be representative of the extensive genus of any primer pair that can amplify the magnitude of nucleic acids discussed above.

Applicants' arguments center around the structure of SEQ ID NO: 7 and assert that because this sequence is known, it would have been well within the knowledge of one skilled in the art to use this sequence as a basis for design of hybridizing probes and primer pairs. The Office does not disagree that an isolated nucleic acid consisting of the nucleotide sequence of SEQ ID NO: 7 from nucleotides 15-1652, an isolated nucleic acid consisting of the full length complement of the nucleotide sequence of SEQ ID NO: 7; and an isolated nucleic acid encoding the polypeptide of SEQ ID NO: 8 have adequate written description in the specification as filed. Applicants further contend that because the specification sets forth the words now claimed in claim 5, for example, that adequate written description has been provided based upon the exemplary nucleic acid of SEQ ID NO: 7 from nucleotides 15-1652. In other words, Applicants submit that possession of a nucleic acid molecule consisting of SEQ ID NO: 7 from nucleotides 15-1652 and encoding a polypeptide consisting of SEQ ID NO: 8 is adequate to place Applicants in possession of the broad genus of the instantly claimed nucleic acid molecules. However, a mere statement that a genus of nucleic acid molecules is a part of the invention does not constitute an adequate written description of those nucleic acid molecules. Since the various nucleic acid molecules do not possess defined structures, fragments or variants of these nucleic acid molecules also lack adequate written description, and so also vectors and host cells comprising the same. Furthermore, since the sole purpose of the instant invention is to use the claimed nucleic acid segment and variant species for diagnostic or therapeutic applications, i.e., as probes, primers or pharmaceutical compositions, any segment or variant species encompassed within the claimed genus is required to be functional, i.e., is at least required to retain of the 'specificity to *Streptococcus pyogenes*'. Other than the structure and function(s) of one nucleic acid species, i.e., SEQ ID NO: 7 which encodes a functional polypeptide of SEQ ID NO: 8, the structure of a representative number of functional (i.e., *S. pyogenes*-specific) nucleic acid variant or segment species that are currently encompassed within the claimed genus is not adequately described. A

nucleic acid comprising a nucleotide sequence that is identical to a segment comprising at least 25% of contiguous nucleotide bases of SEQ ID NO: 7 from nucleotides 15-1652 is neither shown to be *S. pyogenes*-specific such that it has diagnostic applications for detecting *S. pyogenes* strains or *S. pyogenes* infections/diseases, nor is it predictable that such nucleic acid molecules or segments would remain *S. pyogenes*-specific simply by virtue of having sequence identity to 25% of contiguous nucleotide bases of SEQ ID NO: 7 from nucleotides 15-1652. The specification provides no guidance as to which specific nucleotides must be retained in a variant or segment, or which may be varied without causing any detrimental effect to the specificity of the claimed molecule or the protein or polypeptide that it encodes. While one of skill in the art would be able to do the simplest math and determine how many nucleotides constitute at least 25% of the nucleotides from the recited region of SEQ ID NO: 7, without specific guidance, one of skill in the art would not be able to identify a representative number of such nucleic acid variant or segment species that retains *S. pyogenes*-specificity. There is lack of description as to which 'at least 25% contiguous nucleotide bases' of SEQ ID NO: 7 from nucleotides 15-1652 should be retained within a nucleic acid molecule such that it would serve as a *S. pyogenes*-specific primer or probe. Similarly, the precise structure of a representative number of nucleic acid molecule species which encode *S. pyogenes*-specific functional polypeptide variant species that are at least 95%, 97% and 98% homologous to the polypeptide of SEQ ID NO: 8 is not described. This is particularly critical because of the art-known conservation among heat shock proteins of microbial and non-microbial origin and the common existence of undesired auto-immunogenic segments within the HSP nucleic acid and HSP polypeptide molecules. There is no adequate description in the instant specification with regard to which variations, i.e., insertions, deletions, additions and substitutions, in the claimed molecule would result in a variant or segment that would retain the functional integrity or biological/immunogenic competence or specificity of the molecule, or the protein or polypeptide that it encodes, without rendering it non-functional. As set forth previously, a mere statement in the paragraph bridging pages 5 and 6 of the specification that the invention includes an isolated nucleic acid molecule comprising a nucleotide sequence that is identical to a segment comprising at least 25% of contiguous nucleotide bases of SEQ ID NO: 7 from nucleotides 15-1652 or a complement thereof, or an isolated nucleic acid molecule encoding a variant Hsp60 that is at least 95%, 97% or 98% homologous to a polypeptide

of SEQ ID NO: 8 is insufficient to meet the written description provisions of 35 U.S.C § 112, first paragraph. As set forth in paragraph 12 of the Office Action mailed 06/06/03, the *Written Description Guidelines* state:

> There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between the structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function.

The description provided for the species, SEQ ID NO: 7 and 8, is insufficient description for the whole genus that includes the various claimed segment or variant species. The Hsp60 polypeptide of *S. pyogenes* has specific biological properties dictated by the structure of the polypeptide and the corresponding structure of the structural gene sequence which encodes it. There has to be some nexus between the structure of the gene sequence, the structure of the polypeptide encoded, and the function of the encoded polypeptide. The function cannot be predicted from the modification of the structure of the gene and in the instant case, the DNA encoding the polypeptide variant. Applicants have not shown that modification of a reference nucleotide sequence encoding a polypeptide variant as claimed would automatically predict the production of a Hsp60 polypeptide variant specific to *S. pyogenes* as disclosed. Given that a single amino acid substitution or deletion can alter the functions or specificity of a given protein or polypeptide, a dissimilarity as high as at least 5%, 3% or 2% in the encoded polypeptide is not expected to yield a functional or *S. pyogenes*-specific polypeptide variant of SEQ ID NO: 8. Regardless of the complexity or simplicity of the method of isolation, conception cannot be achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that it is a part of the invention and a reference to a potential method of isolating it. The functional nucleic acid variant itself is required. See *Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993)* and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.* See Written Description Requirement, *Federal Register*, vol. 66, no. 4, Notices, pp. 1099-1111, 05 January 2001). The rejection stands.

**21)** The rejection of claim 2 made in paragraph 15 of the Office Action mailed 06/06/03 under 35 U.S.C § 102(b) as being anticipated by Hamel *et al.* (WO 96/40928, already of record), is maintained for reasons set forth therein and herebelow.

Applicants contend that the test for anticipation is one of identity and that a prior art reference must disclose exactly what is claimed. Applicants state that Hamel does not disclose "*the*

*sequence* of claim 2" [Emphasis added], but teaches Hsp70 having SEQ ID NO: 19 and 20. Applicants assert that these sequences are different than those of the Hsp60 encoded by the nucleic acid molecule of claim 2. Applicants state that the nucleic acids disclosed by Hamel and those disclosed by Applicants are structurally and functionally distinct. Applicants submit the reference of Parsell *et al.*, 1993 and state that hsp70 and hsp60 are distinct families.

Applicants' arguments have been carefully considered, but are non-persuasive. The term 'Hsp60', as recited broadly and vaguely in the claim, encompasses a protein, polypeptide, peptide, or a protein fragment, or a protein variant which is encoded by an isolated nucleic acid of *Streptococcus pyogenes*. Claim 2 does not place a structural limit on the claimed nucleic acid molecule encoding a *Streptococcus pyogenes* Hsp60. The specification on page 11 describes that 'it should be understood that Hsp60 includes ... variants ...and fragments of the native protein sequence' and that 'such variants differ ..... by one or more amino acid substitutions, insertions, deletions, or the like'. With regard to Applicants' mentioning of "*the sequence* of claim 2", contrary to Applicants' assertion, the instant claim 2 does not include the term 'the sequence'. In view of the lack of structure, i.e., SEQ ID number, for the recited Hsp60 in the claim, the prior art Hsp is deemed to meet the claim limitations. The limitation 'Hsp60' is viewed merely as a different name given to the prior art product and does not impart any structure or function that distinguishes the product of the prior art from the claimed product. Hamel *et al.* disclosed a nucleotide sequence derived from *Streptococcus pyogenes* that encodes a heat shock protein (see abstract; page 75-77; and claims). The prior art nucleotide sequence is derived from *Streptococcus pyogenes* and it encodes a heat shock protein, and therefore it qualifies as a variant having more than one amino acid substitutions, deletions, insertions etc. The rejection stands.

**New Rejection(s)**

Applicants are asked to note the new rejection(s) made in this Office Action. Applicants' amendments and/or the submission of new claims necessitated the new ground(s) of rejection presented in this Office Action.

**Rejection(s) under 35 U.S.C § 112, Second Paragraph**

**22)** Claims 7, 19-24, 31 and 41-45 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant

regards as the invention.

(a) Claim 7, as amended, is vague in the recitation: 'encoding a polypeptide that is selectively bound by an antibody specific for a *Streptococcus pyogenes* Hsp60', because it is unclear how a nucleic acid can encode a polypeptide bound by an antibody.

(b) Claim 41 is vague and indefinite in the recitation: 'nucleic acid molecule consisting of .... nucleotides that hybridizes to SEQ ID NO: 7 from nucleotides 15-1652'. A nucleic acid molecule 'consisting of' nucleotides (contiguous or discontiguous) is a double-stranded molecule and therefore, it is unclear how such a double-stranded nucleic acid molecule can hybridize to SEQ ID NO: 7 from nucleotides 15-1652, which is also double-stranded. It is unclear how sense strands can hybridize to sense strands as opposed to anti-sense strands.

(c) Claims 19-24 and 31, which depend directly or indirectly from claim 7, and claims 42-45, which depend directly or indirectly from claim 41, are also rejected as being indefinite because of the indefiniteness or vagueness identified above in the base claim.

**Rejection(s) under 35 U.S.C § 102**

**23)** Claims 3, 5, 19-24, 31 and 40-45 are rejected under 35 U.S.C § 102(e) as being anticipated by Kunsch *et al.* (US 6,420,135, filed 10/31/1996).

It is noted that the complementary nucleotide sequence claimed in claim 3(c) and claims 5 and 40(c) does not have a size limit, and therefore encompasses nucleotide sequences that are both partially and fully complementary to the recited nucleic acid molecule.

Kunsch *et al.* taught an isolated nucleic acid molecule consisting of 6 or more nucleotides of SEQ ID NO: 1-39 and complementary sequences thereto operably associated with a regulatory sequence that controls gene expression (see abstract; claims; third paragraph in column 9; fourth paragraph in column 4; last paragraph in column 3; and sixth paragraph in column 25). Diagnostic fragments (DF) of nucleic acid molecules with 17 contiguous nucleotide bases that selectively hybridize to *S. pneumoniae* sequences; expression vectors comprising the nucleic acid fragments; and host cells comprising such nucleic acid molecules are taught (see fifth paragraph in column 13; first paragraph in column 14; third and fourth paragraphs in column 15; and paragraph bridging columns 16 and 17). Diagnostic primers and probes with 18 nucleotide bases that recognize the *S. pneumoniae* nucleotide sequences under high stringency conditions, such as, 65°C in 6 x SSC, and

kits containing such primers or probes and reagents such as PBS (i.e., pharmaceutically acceptable carrier or diluent) or Tris-buffers are taught (see third and fourth paragraphs in column 19; second paragraph in column 14; second full paragraph in column 35; and column 24). The attached sequence search report is provided to show stretches of contiguous nucleotide bases in the prior art nucleotide sequence that consist of 17 or 18 bases that are 100% structurally identical with fragments of the instantly recited SEQ ID NO: 7. The disclosed nucleic acid molecule is expected to serve as a complementary sequence to the nucleotide sequence of SEQ ID NO: 7 in the region from nucleotides 15 to 1652.

Claims 3, 5, 19-24, 31 and 40-45 are anticipated by Kunsch *et al.*

**24)** Claims 3 and 40 are rejected under 35 U.S.C § 102(b) as being anticipated by Probeski (GenEmbl accession number X89236, submitted 06/29/1995).

Probeski taught an isolated groEL gene of the heat shock protein 60 of *S. pyogenes* having more than 86% sequence identity with the instantly recited nucleotide sequence of SEQ ID NO: 7 from nucleotides 15-1652 and 100% local sequence identity with long contiguous stretches of the instantly recited nucleotide sequence of SEQ ID NO: 7 from nucleotides 15-1652. The prior art nucleotide sequence therefore comprises or serves as a sequence that is complementary to the instantly claimed nucleotide sequence.

Claims 3 and 40 are anticipated by Probeski.

**Relevant Art**

**25)** The relevant art made of record and not relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- Lemos *et al.* (*J. Med. Microbiol.* 47: 711-715, 1998) taught heat shock proteins expressed by *Streptococcus pyogenes* (see entire document).

**Objection(s)**

**26)** Claims 19, 21-24, 31, 33, 35 and 40 are objected to for the following reasons:

(a) New claim 40 is objected to for including non-elected subject matter and for being dependent from a rejected claim.

(b) Claims 33 and 35 are objected to for being dependent from a rejected claim.

(c) Claims 19, 21-24 and 31 are objected to for including or for being dependent from a

claim that includes non-elected subject matter.

**Remarks**

**27)** Claims 2, 3, 5-7, 19-24, 31 and 38-45 stand rejected. Claims 33 and 35 stand objected to.

**28)** Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

**29)** Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

**30)** Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. The Examiner can normally be reached on Monday to Friday from 7.45 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

June 04

S. DEVI, PH.D.
PRIMARY EXAMINER

T 3
961-527-77
ce 77, Application US/08961527
No. 6420135
ERAL INFORMATION:
APPLICANT: Charles Kunsch
TITLE OF INVENTION: Streptococcus pneumoniae Polynucleotides and Sequences
NUMBER OF SEQUENCES: 391
CORRESPONDENCE ADDRESS:
ADDRESSEE: Human Genome Sciences, Inc.
STREET: 9410 Key West Avenue
CITY: Rockville
STATE: Maryland
COUNTRY: USA
ZIP: 20850
COMPUTER READABLE FORM:
MEDIUM TYPE: Diskette, 3.50 inch, 1.4Mb storage
COMPUTER: HP Vectra 486/33
OPERATING SYSTEM: MSDOS version 6.2
SOFTWARE: ASCII Text
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/08/961,527
FILING DATE:
CLASSIFICATION: 424
PRIOR APPLICATION DATA:
APPLICATION NUMBER:
FILING DATE:
ATTORNEY/AGENT INFORMATION:
NAME: Brookes, A. Anders
REGISTRATION NUMBER: 36,373
REFERENCE/DOCKET NUMBER: PB340P1
TELECOMMUNICATION INFORMATION:
TELEPHONE: (301) 309-8504
TELEFAX: (301) 309-8512
INFORMATION FOR SEQ ID NO: 77:
SEQUENCE CHARACTERISTICS:
LENGTH: 5365 base pairs
TYPE: nucleic acid
STRANDEDNESS: double
TOPOLOGY: linear
US-08-961-527-77

SEQ ID NO 7

Query Match 63.2%; Score 1034.4; DB 4; Length 5365;
Best Local Similarity 77.4%; Pred. No. 1.7e-294;
Matches 1254; Conservative 0; Mismatches 366; Indels 0; Gaps 0;

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Qy          1 ATGGCAAAAGAAATCAAATTTTCAGCAGATGCGCGTGCTGCCATGGTGCGCGGAGTTGAT 60
              ||| |||||||||| |||||||| |||||| ||| | |||||||| || || || |||
Db        278 ATGTCAAAAGAAATTAAATTTTCATCAGATGCCCGTTCAGCCATGGTTCGTGGTGTCGAT 337

Qy         61 ATGTTAGCAGATACCGTCAAAGTAACGCTTGGTCCTAAAGGGCGCAATGTTGTTCTTGAA 120
              ||  | ||||| || || |||||||  | || || ||||| |||||||| |||||||||
Db        338 ATCCTTGCAGACACTGTTAAAGTAACCTTGGGACCAAAAGGTCGCAATGTCGTTCTTGAA 397
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SEQ ID NO. 7 (continued)